



RespireRx Pharmaceuticals Inc. Establishes Research Collaboration With University College London to Study the Use of AMPAkinines for the Treatment of GRIA Disorders

Glen Rock, N.J., April 5, 2023 /Globe Newswire - RespireRx Pharmaceuticals Inc. (OTC Markets: RSPI) ("RespireRx" or the "Company"), a leader in the discovery and development of innovative and revolutionary treatments to combat diseases caused by disruption of neuronal signaling, is pleased to announce the entering into a material transfer agreement with University College London (UCL) as part of a collaborative research effort involving Dr. Ian Coombs and Prof. Mark Farrant, founder members of the GRIA Scientific Advisory Board of the CureGRIN Foundation ("CureGRIN") and from the UCL Department of Neuroscience, Physiology, and Pharmacology. The UCL group, which also includes Prof. Stuart Cull-Candy F.R.S., has been awarded funding from CureGRIN, and will be working with the RespireRx research team to study the possibility of using CX1739, RespireRx's lead clinical AMPAkinine, for the treatment of a major class of GRIA disorders.

GRIA Disorder refers to a family of rare genetic diseases caused by mutations in the AMPA glutamate receptor genes that cause either a loss or gain in the functioning of these receptors, which are the site of action of RespireRx's AMPAkinines and which play an important role in learning and memory as well as other critical biological functions (see <https://curegrin.org/what-are-gri-disorders/> for a description of these disorders). Dr. Coombs's work seeks to characterize the genetic variants underlying the diverse behavioral and cognitive symptoms in children with GRIA Disorder and use this knowledge to create a diagnostic method to determine on a molecular level which patients have a decline or gain in the functioning of these receptors and use this diagnostic to choose what drugs to use to restore normal function.

"It is very important to characterize the properties of AMPA receptor variants which underly the diverse symptoms displayed by children with GRIA Disorder in order to better determine which drugs could act as potential treatments. Evidence suggests that the majority of these disease-associated variants produce underactive AMPARs so I am very excited to be working with the AMPAkinine CX1739, which boosts AMPA receptor function, to determine on a molecular level its potential as a precision therapy for children with GRIA Disorder, for whom no truly effective treatment presently exists," said Dr. Coombs.

"It is the ultimate intention of this collaboration to test CX1739 in patients with specific variants that we demonstrate produce a decline in function of the AMPA receptor. Positive therapeutic effects with RespireRx's AMPAkinines already have been reported in animal mutations modelling related disorders such as Pompe that also suffer from declines in AMPA receptor functioning. AMPAkinines may have the potential to treat a broad range of patients suffering from AMPA receptor dysfunction," commented Dr. Arnold Lippa, RespireRx Executive Chairman, Chief Executive Officer, President and Chief Scientific Officer.

The RespireRx team that will collaborate with Dr. Coombs, Prof. Farrant and Prof. Cull-Candy includes Drs. Jeffrey M. Witkin and Rok Cerne, both of whom are RespireRx Research Fellows in addition to their academic affiliations at The University of Wisconsin-Milwaukee, Ascension St. Vincent Hospital and Indiana University/Purdue University, respectively. The team has extensive expertise and are well known for their work in drug discovery and development, including novel analgesic, anxiolytic, anti-epileptic and anti-depressant drugs.

About RespireRx Pharmaceuticals Inc.

RespireRx Pharmaceuticals Inc. is a leader in the discovery and development of medicines for the treatment of psychiatric and neurological disorders, with a focus on treatments that address conditions affecting millions of people, but for which there are few or poor treatment options, including obstructive sleep apnea ("OSA"),

attention deficit hyperactivity disorder (“ADHD”), epilepsy, pain, recovery from spinal cord injury (“SCI”), and certain neurological orphan diseases. RespireRx is developing a pipeline of new and re-purposed drug products based on our broad patent portfolios for two drug platforms: (i) pharmaceutical cannabinoids, which include dronabinol, a synthetic form of Δ -9-tetrahydrocannabinol (“ Δ -9-THC”) that acts upon the nervous system’s endogenous cannabinoid receptors and (ii) neuromodulators, which include AMPAkines and GABAkines, proprietary chemical entities that positively modulate (positive allosteric modulators or “PAMs”) AMPA-type glutamate receptors and GABA_A receptors, respectively.

The Company holds exclusive licenses and owns patents and patent applications or rights thereto for certain families of chemical compounds that claim the chemical structures and their uses in the treatment of a variety of disorders, as well as claims for novel uses of known drugs.

EndeavourRx: Neuromodulators

GABAkines. Under a License Agreement with the University of Wisconsin-Milwaukee Research Foundation, Inc. (“UWMRF”) and on behalf of its EndeavourRx business unit, RespireRx has licensed rights to certain selectively acting GABAkines because of their ability to selectively amplify inhibitory neurotransmission at a highly specific, subset of GABA_A receptors, thus producing a unique efficacy profile with reduced side effects. Preclinical studies have documented their efficacy in a broad array of animal models of interrelated neurological and psychiatric disorders including epilepsy, pain, anxiety, and depression in the absence of or with greatly reduced propensity to produce sedation, motor-impairment, tolerance, dependence and abuse. The Company currently is focusing on developing KRM-II-81 for the treatment of epilepsy and pain.

KRM-II-81 has displayed a high degree of anti-convulsant activity in a broad range of preclinical studies, including in treatment resistant and pharmaco-resistant models. Not only was KRM-II-81 highly effective in these models, but pharmaco-resistance or tolerance did not develop to its anti-convulsant properties. These latter results are particularly important because pharmaco-resistance occurs when medications that once controlled seizures lose efficacy as a result of chronic use and it is a principal reason some epileptic patients require brain surgery to control their seizures. In support of its potential clinical efficacy, translational studies have demonstrated the ability of KRM-II-81 to dramatically reduce epileptiform electrical activity when administered in situ to brain slices excised from treatment resistant epileptic patients undergoing surgery.

In addition, KRM-II-81 has displayed a high degree of analgesic activity in a broad range of preclinical studies. In intact animal models of pain, the analgesic efficacy of KRM-II-81 was comparable to or greater than commonly used analgesics. At the same time, KRM-II-81 did not display side effects such as sedation and motor impairment, but even more importantly, it did not produce tolerance, dependence, respiratory depression or behavioral changes indicative of abuse liability, which are produced by opioid narcotics and are at the heart of the opioid epidemic.

The Company has developed a series of back-up compounds to KRM-II-81.

AMPAkines. Through an extensive translational research effort from the cellular level through Phase 2 clinical trials, the Company has developed a family of novel, low impact AMPAkines, including CX717, CX1739 and CX1942 that may have clinical application in the treatment of CNS-driven neurobehavioral and cognitive disorders, spinal cord injury, neurological diseases, and certain orphan indications. Our lead clinical compounds, CX717 and CX1739, have successfully completed multiple Phase 1 safety trials. Both compounds have also completed Phase 2 proof of concept trials demonstrating target engagement, by antagonizing the ability of opioids to induce respiratory depression.

AMPAkines have demonstrated positive activity in animal models of ADHD, results that have been extended translationally into statistically significant improvement of symptoms observed in a Phase 2 human clinical trial of CX717 in adult patients with ADHD. Statistically significant therapeutic effects were observed within one week. We believe AMPAkines may represent a novel, non-stimulant treatment for ADHD with a more rapid onset of action than alternative non stimulants, such as Straterra® (atomoxetine), and without the drawbacks of amphetamine-type stimulants.

In a series of important studies funded by grants from the National Institutes of Health and published in a number

of peer reviewed articles, Dr. David Fuller (University of Florida), a long-time RespireRx collaborator, has demonstrated the ability of CX1739 and CX717, the Company's lead AMPAkinines, to improve motor nerve activity and muscle function in a number of animal models of spinal cord injury (SCI).

ResolutionRx: Pharmaceutical Cannabinoids.

ResolutionRx Ltd (Australian Company Number a/k/a ACN 664 925 651) was formed in Australia on January 11, 2023 by RespireRx as an unlisted public company. RespireRx intends to contribute, sub-license, assign or otherwise make available to ResolutionRx, its cannabinoid drug development program subject to certain liabilities. ResolutionRx would then engage in the research and development ("R&D") associated with that program, initially for the development of a new formulation of dronabinol for use in a Phase 3 clinical trial and the filing of regulatory approval for the treatment of OSA. The current total budget for that program over the next several years is approximately US\$16.5 million, most, but not all of which is expected to be eligible for the Australian R&D tax refund. Dronabinol, a synthetic version of Δ -9-THC, a naturally occurring substance in the cannabis plant, has already demonstrated significant improvement in the symptoms of OSA in two Phase 2 clinical trials. OSA is a serious respiratory disorder that is estimated to be between 29.4 and 54.1 million people in the United States (American Association of Sleep Medicine and Lancet, respectively) and has been linked to increased risk for hypertension, heart failure, depression, and diabetes. There are no approved drug treatments for OSA.

Because dronabinol is already FDA approved for the treatment of AIDS related anorexia and chemotherapy induced nausea and vomiting, the Company further believes that its re-purposing strategy would only require approval by the FDA of a 505(b)(2) new drug application ("NDA"), an efficient regulatory pathway that allows the use of publicly available data.

Additional information about RespireRx and the matters discussed herein can be obtained on the Company's web-site at www.respirerx.com or in the Company's filings with the Securities and Exchange Commission at www.sec.gov.

Not a Securities Offering or Solicitation

This communication shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sales of securities in any jurisdiction in which such offer, solicitation or sale of securities would be unlawful before registration or qualification under the laws of such jurisdiction.

Cautionary Note Regarding Forward-Looking Statements

This press release contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the Company intends that such forward-looking statements be subject to the safe harbor created thereby. These might include statements regarding the Company's future plans, targets, estimates, assumptions, financial position, business strategy and other plans and objectives for future operations, and assumptions and predictions about research and development efforts, including, but not limited to, preclinical and clinical research design, execution, timing, costs and results, future product demand, supply, manufacturing, costs, marketing and pricing factors.

In some cases, forward-looking statements may be identified by words including "assumes," "could," "ongoing," "potential," "predicts," "projects," "should," "will," "would," "anticipates," "believes," "intends," "estimates," "expects," "plans," "contemplates," "targets," "continues," "budgets," "may," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words, and such statements may include, but are not limited to, statements regarding (i) future research plans, expenditures and results, (ii) potential collaborative arrangements, (iii) the potential utility of the Company's product candidates, (iv) reorganization plans, and (v) the need for, and availability of, additional financing. Forward-looking statements are based on information available at the time the statements are made and involve known and unknown risks, uncertainties and other factors that may cause our results, levels of activity, performance or achievements to be materially different from the information expressed or implied by the forward-looking statements in this press release.

These factors include but are not limited to, regulatory policies or changes thereto, available cash, research and development results, issuance of patents, competition from other similar businesses, interest of third parties in collaborations with us, and market and general economic factors, and other risk factors disclosed in “Item 1A. Risk Factors” in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on April 15, 2022 (the “2021 Form 10-K”).

You should read these risk factors and the other cautionary statements made in the Company’s filings as being applicable to all related forward-looking statements wherever they appear in this press release. We cannot assure you that the forward-looking statements in this press release will prove to be accurate and therefore prospective investors, as well as potential collaborators and other potential stakeholders, are encouraged not to place undue reliance on forward-looking statements. You should read this press release completely. Other than as required by law, we undertake no obligation to update or revise these forward- looking statements, even though our situation may change in the future.

We caution investors, as well as potential collaborators and other potential stakeholders, not to place undue reliance on any forward-looking statement that speaks only as of the date made and to recognize that forward-looking statements are predictions of future results, which may not occur as anticipated. Actual results could differ materially from those anticipated in the forward-looking statements and from historical results, due to the risks and uncertainties described in the 2021 Form 10-K and in this press release, as well as others that we may consider immaterial or do not anticipate at this time. These forward-looking statements are based on assumptions regarding the Company’s business and technology, which involve judgments with respect to, among other things, future scientific, economic, regulatory and competitive conditions, collaborations with third parties, and future business decisions, all of which are difficult or impossible to predict accurately and many of which are beyond the Company’s control. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we do not know whether our expectations will prove correct. Our expectations reflected in our forward-looking statements can be affected by inaccurate assumptions that we might make or by known or unknown risks and uncertainties, including those described in the 2021 Form 10-K and in this press release. These risks and uncertainties are not exclusive and further information concerning us and our business, including factors that potentially could materially affect our financial results or condition, may emerge from time to time.

For more information about the risks and uncertainties the Company faces, see “Item 1A. Risk Factors” in our 2021 Form 10-K. Forward-looking statements speak only as of the date they are made. The Company does not undertake and specifically declines any obligation to update any forward-looking statements or to publicly announce the results of any revisions to any statements to reflect new information or future events or developments. We advise investors, as well as potential collaborators and other potential stakeholders, to consult any further disclosures we may make on related subjects in our annual reports on Form 10-K and other reports that we file with or furnish to the SEC.

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